Figure S1 Bile acid pathways are altered in cachectic mice. (A) Ileal expression of *Fgf15* by qPCR and **(B)** portal levels of FGF15 by western blot analysis in C26-transplanted mice (C26) as compared to sham-injected mice (CT).
Fgf15, Fibroblast growth factor 15.
N=7-8 mice/group, data are presented as mean ± SEM, *p<0.05, ***p<0.001.

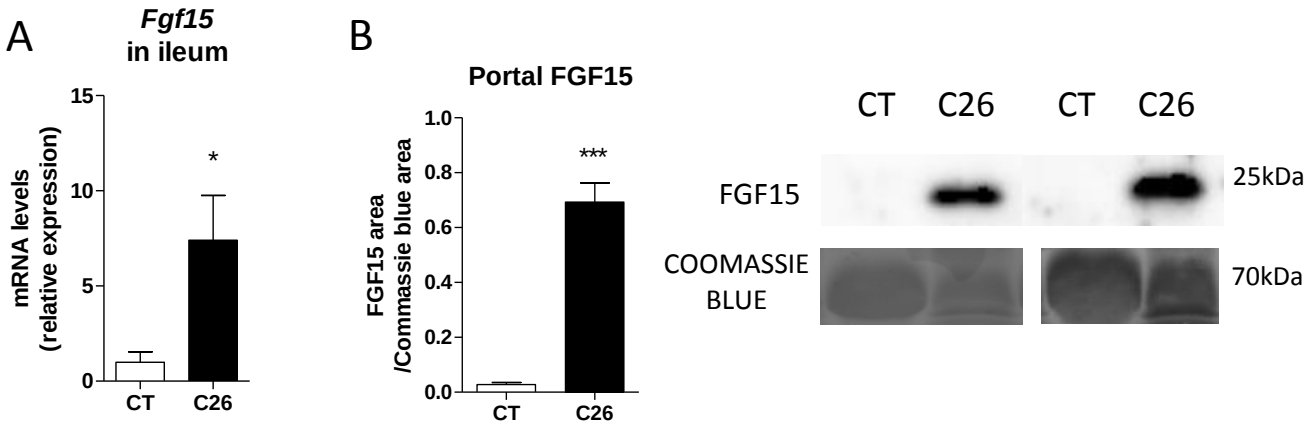

Figure S2 Hematoxylin and eosin-stained liver sections of control (CT) and cachectic mice (C26).
Arrows indicate inflammatory cells. Scale of 100 µm, magnitude 10X.

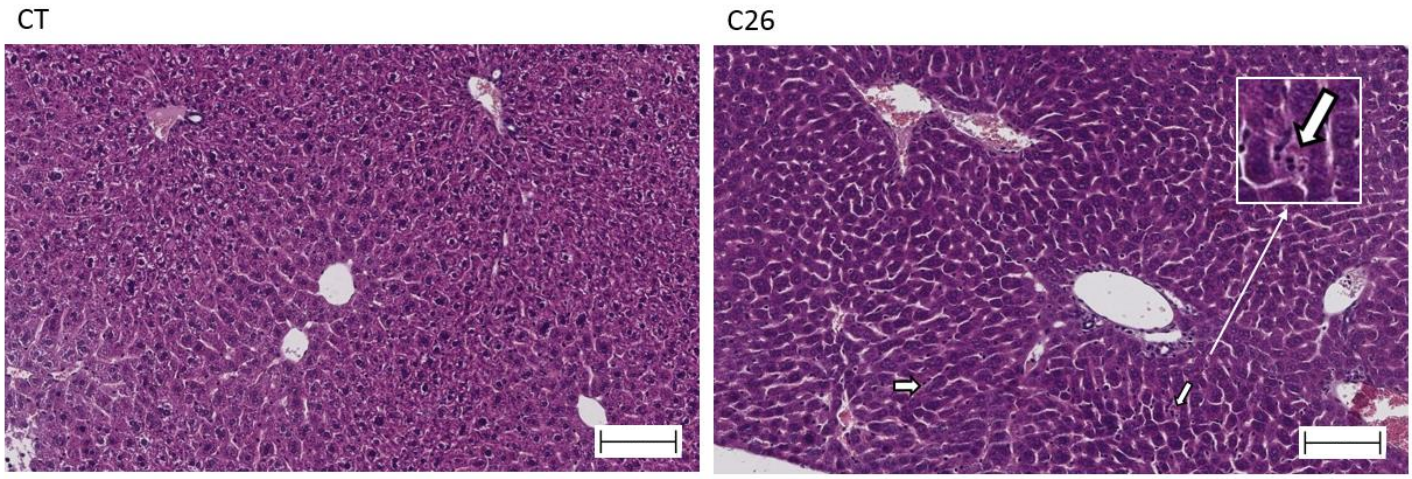

Figure S3 Progression of the cachectic features and hepatic alterations in cachectic mice. (A) Body weight and food intake evolution, subcutaneous (SAT), brown adipose tissue (BAT) and gastrocnemius (GAS) weight evolution at 8, 9 and 10 days after C26 cell injection (C26) or sham-injected mice (CT). Evolution of gene expression levels involved in muscle atrophy in the gastrocnemius **(B)** and hepatic alterations **(C)** at 8, 9 and 10 days after injection.
N=7-8 mice/group, data are presented as mean ± SEM, *p<0.05, **p<0.01, ***p<0.001 vs CT group.

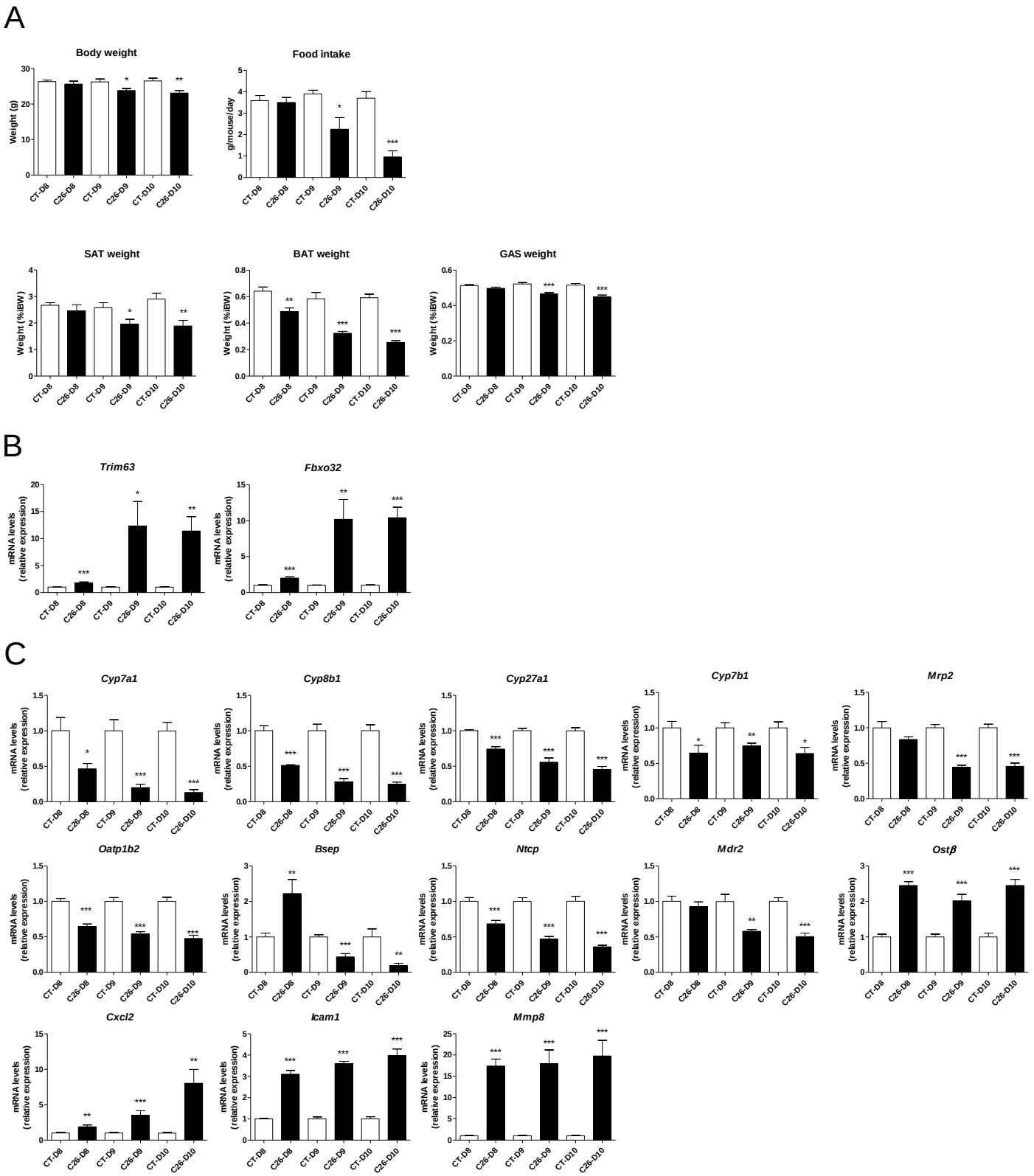

Figure S4 Evolution of bile acid profile in the liver of C26 cachectic mice. (A) Hepatic total bile acid levels and **(B)** bile acid profile in mice at 8, 9 and 10 days after C26 cell injection (C26) or sham-injection (CT).
N=7-8 mice/group, data are presented as mean ± SEM, *p<0.05, **p<0.01, ***p<0.001 vs CT group.

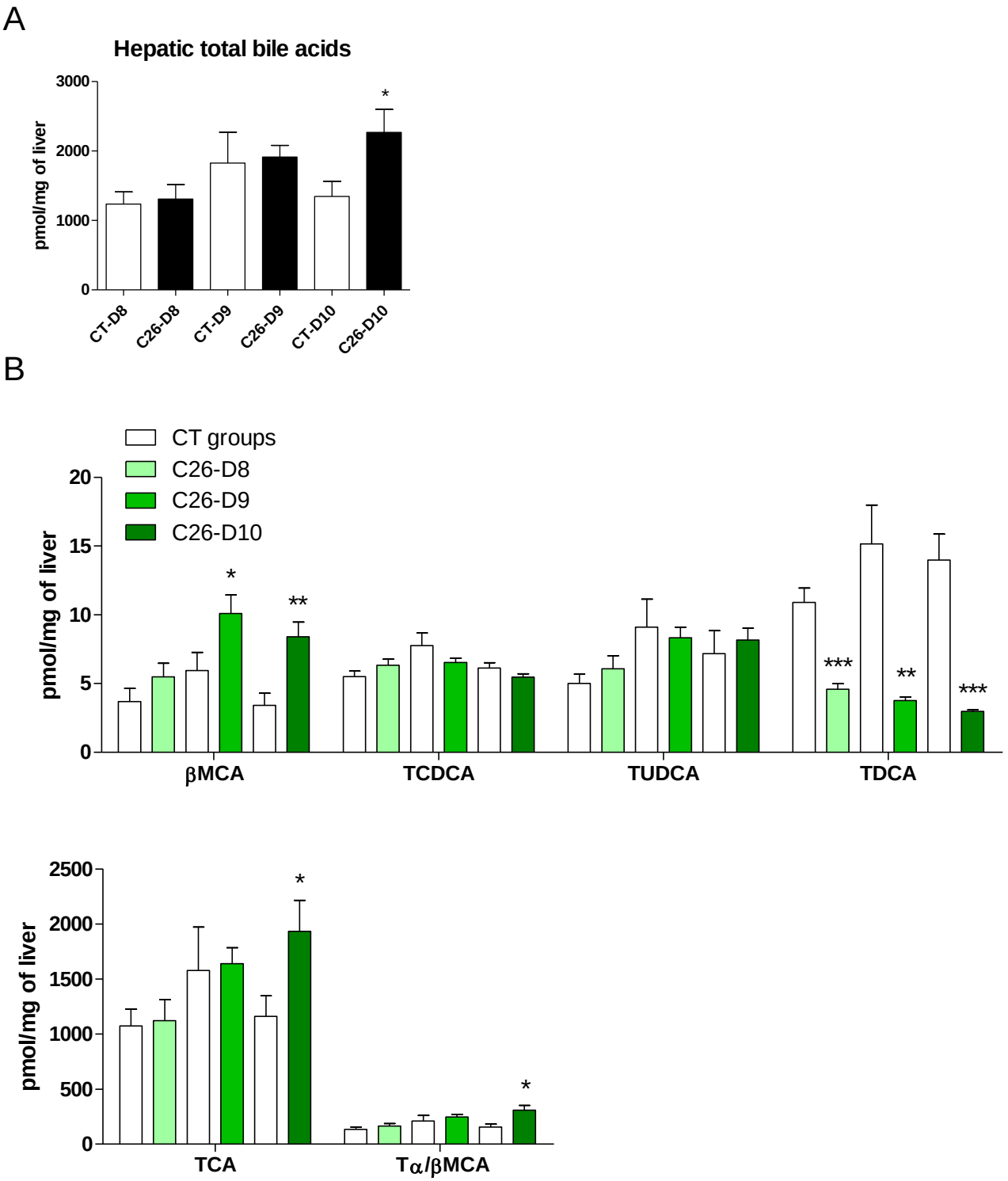

Figure S5 Minor effects of cholestyramine treatment on muscle atrophy and thermogenesis in cachectic mice (A) Expression level of *Fgf15* in the ileum of sham-injected mice (CT), in untreated C26-transplanted mice (C26) and in C26-transplanted mice receiving cholestyramine in their diet (C26-CHO). **(B)** Tumor weight in C26 and C26-CHO, as well as food intake evolution of CT, C26 and C26-CHO mice. ***p<0.001 vs CT. **(C)** Body weight evolution and body weight kinetic between day 8 and 10 after cell injection in CT, C26 and C26-CHO mice. (left; ***p<0.001 vs CT) (right; ***p<0.001 vs CT; #p<0.05 and ###p<0.001 vs C26). **(D)** Expression levels of genes involved in muscle atrophy in the gastrocnemius of CT, C26 and C26-CHO mice. **(E)** Expression levels of genes involved in brown adipose tissue thermogenesis in the brown adipose tissue of CT, C26 and C26-CHO mice.

Fgf15, Fibroblast growth factor 15; *Map1lc3a*, Microtubule Associated Protein 1 Light Chain 3 Alpha; *Trim63*, Tripartite Motif Containing 63 (also known as Murf1); *Fbxo32*, F-Box Protein 32 (also known as Atrogin1); *Ctsl*, Cathepsin L; *Dio2*, iodothyronine deiodinase 2; *Ucp1*, uncoupling protein 1; *Acox1*, Acyl-CoA oxidase 1; *Cidea*, cell death inducing DFFA like effector a; *Gk*, glycerol kinase; *Lpl*, lipoprotein lipase.

N=7-8 mice/group, data are presented as mean ± SEM, *p<0.05, **p<0.01, ***p<0.001 vs C26.

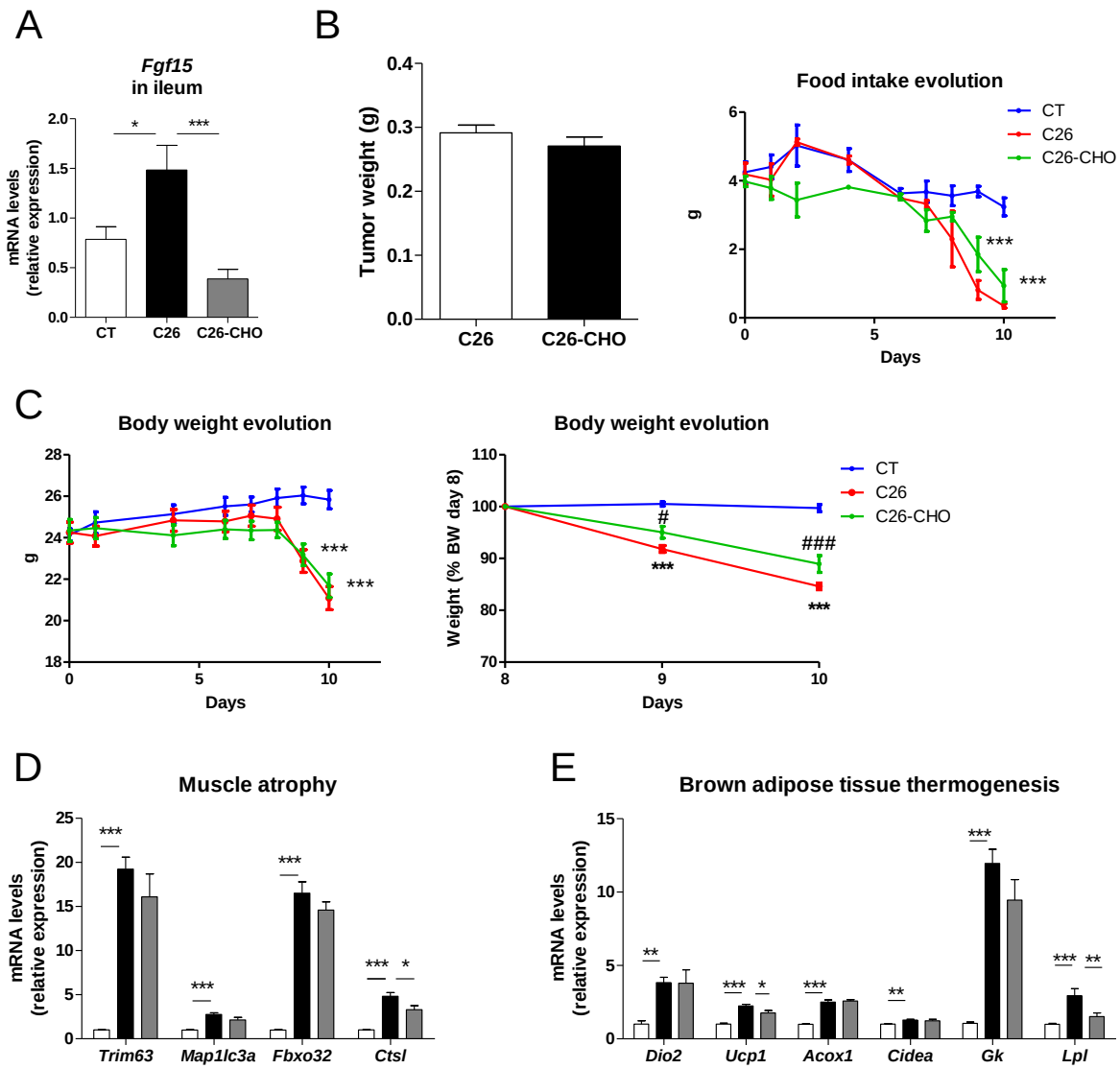

Figure S6 Reduced food intake is not the main driver of hepatic alterations in cachectic mice.

(A) mRNA expression of genes involved in bile acid metabolism and inflammation in the liver. **(B)** mRNA expression of *Fgf15* in the ileum.

Mice were either sham-injected (CT), transplanted with cancer cells (C26), sham-injected and pair-fed to CT mice (CT-PF) or sham-injected and pair-fed to C26 mice (C26-PF). *Cyp7b1*, cytochrome P450 family 7 subfamily B member 1; *Cyp8b1*, cytochrome P450 family 8 subfamily B member 1; *Ntcp*, Na(+)/taurocholate transport protein; *Bsep*, Bile Salt Export Pump; *Cxcl2*, C-X-C motif chemokine ligand 2; *Icam1*, intercellular adhesion molecule 1; *Fgf15,* Fibroblast growth factor 15.

N=7-8 mice/group, data are presented as mean ± SEM, *p<0.05, **p<0.01, ***p<0.001.